REMARKS

With entry of this amendment, claims 2-9, 11, and 22-25 are pending in the instant application. The specification is amended to reflect the current status of U.S. Application No. 09/823,033, filed March 29, 2001. In addition, claims 12, 13, and 26 are canceled and claims 6, 11, 22, and 24 are amended as set forth in detail herein. No new matter is added. Applicants reserve the right to prosecute claims to cancelled subject matter in one or more continuing applications. In view of these amendments and the following remarks, reconsideration of the application is respectfully requested.

Claim Amendments

Independent claims 11 and 22 have been amended to further expedite prosecution of this application by substantially incorporating the limitation recited in dependent claims 12 and 26. Accordingly, claims 11 and 22 now specify that each of the first and second polypeptide chains "[consist] of residues X-345 of SEQ ID NO:2, wherein X is an integer from 226 to 235, inclusive." In view of these amendments, dependent claims 12 and 26 have been canceled. Claim 13 has also been canceled to avoid any inconsistency with claim 11 as currently amended.

Claims 6 and 24 have been amended to correct a typographical error by substituting "bone-targeting" for "bone-targetting."

Formal Matters

Priority Determination

The Examiner alleges that, with the exception of U.S. Patent Application No. 09/823,033, filed March 29, 2001, the present claims cannot be entitled to the benefit of the filing dates of the prior applications (namely, U.S. application no. 09/457,066 filed on 12/7/99 and U.S. provisional application nos. 60/193,723 filed on 3/31/00; 60/165,255 filed on 11/12/99; 60/161,653 filed on 10/21/99; 60/142,576 filed on 7/6/99; and 60/111,173 filed on 12/7/98). In particular, the Examiner contends that none of the prior

applications discloses the use of zvegf3 of SEQ ID NO:2 in promoting growth of bone, ligament, or cartilage. Applicants disagree.

Applicants respectfully direct the Examiner's attention to pages 68 and 69 of U.S. provisional application no. 60/111,173, filed December 7, 1998 (the "'173 application"), where certain therapeutic uses of zvegf3 proteins are discussed. In particular, the '173 application states that zvegf3 proteins can be used, *inter alia*, for "fracture repair" as well as for the treatment of wounds such as in cases of compromised wound healing due to "connective tissue disease" (*see* page 68, lines 31 to 37). The '173 application also states that zvegf3 proteins can be used to "promote the growth of tissue damaged by periodontal disease" (*see* page 69, lines 8 and 9), a disease well-known in the art to be characterized by loss of connective tissue structures and bone. Further, the '173 application discloses that among the target cells for zvegf3 are chondrocytes and osteoblasts (*see* page 55, lines 19-28), which are well-known in the art as major cell types of cartilage, ligament, and bone. The above-cited disclosure is also contained in Applicants' provisional applications 60/165,255 (pp. 57 & 72); 60/161,653 (pp. 57 & 71); and 60/142,576 (pp. 56, 68, & 69). Provisional application 60/193,723 also discusses the use of zvegf3 for promoting growth of cartilage, ligament, and bone (*see, e.g.*, p. 5, ll. 26-29; and p. 19, l. 14 to p. 20, l. 6).

In view of the above, it is respectfully submitted that the instant claims – directed, *inter alia*, to the use of zvegf3 in promoting growth of bone, ligament, or cartilage – are supported by each of Applicants' priority applications, including the '173 application filed 12/7/98. For at least these reasons, Applicants respectfully request reconsideration of the Examiner's priority determination.

Objection to the Specification

The specification has been objected to for listing an incorrect status for U.S. Patent Application No. 09/823,033, filed March 29, 2001.

Withdrawal of this objection is respectfully requested in view of Applicants' amendment to the specification to reflect the current status of U.S. Application No. 09/823,033.

Objection to the Claims

Claims 6 and 24 have been objected to for certain typographical errors. Withdrawal of this objection is respectfully requested in view of Applicants' amendments to claims 6 and 24 correcting these errors.

Rejection under 35 U.S.C. § 112

Claim 13 stands rejected under 35 U.S.C. § 112, first paragraph, as allegedly not enabled by the specification. The Examiner contends that the specification does not provide enabling support for the use of a dimeric protein comprising polypeptide chains of residues X-345 of SEQ ID NO:2, wherein X is an integer from 15 to 20.

While Applicants do not agree with this rejection, the rejection is obviated in view of Applicants' cancellation of claims 13, as set forth above.

Rejection under 35 U.S.C. § 102(e)

Claims 2-5, 8, 9, 11, 12, 22, 23, 25 and 26 stand rejected under 35 U.S.C. § 102(e) as allegedly anticipated by US2002/0164687 (Eriksson *et al.*) as evidenced by US 6,934,576 (Camacho *et al.*). The Examiner states that Eriksson discloses a PDGF-C amino acid sequence that is 100% identical to the present SEQ ID NO:2, and further that full length PDGF-C "is likely to be a latent growth factor that needs to be activated by proteolytic processing to release an active PDGF/VEGF homology domain, and that a full putative proteolytic site is found in residues 231-234 in the full length protein." (Office Action at p. 4, last para.) The Examiner goes on to assert, *inter alia*, that Eriksson teaches the use of PDGF-C for "stimulation of connective tissue development," and that stimulating proliferation of osteoblasts or chondrocytes "would be an inherent property once the PDGF-C composition is administered for the purpose of promoting ... growth of connective tissue cells such as bone, ligament, and cartilage." (*Id.* at p. 5.) This rejection is traversed insofar as it pertains to the claims as currently amended.

First, the present claims specify that each of the first and second disulfide-bonded polypeptide chains and chains "consisting of residues X-345 of SEQ ID NO:2,

wherein X is an integer from 226 to 235, inclusive." (*See* independent claims 11 and 22.) Accordingly, the present claims are directed, *inter alia*, to the use of the PDGF-C growth factor domain in the absence of the N-terminal CUB domain. (*See, e.g.*, the instant specification at p. 7, Table 1, which describes the approximate boundaries of the PDGF-C growth factor and CUB domains. *See also* the '173 provisional application at p. 8.)

Further, as set forth above with respect to determination of priority, it is submitted that the instant claims are entitled to the benefit of the '173 provisional application filed 12/7/98. In this regard, only three of Eriksson's priority applications were filed prior to 12/7/98: provisional application nos. 60/102,461 filed 9/30/98; 60/108,109 filed on 11/12/98; and 60/110,749 filed 12/3/98.

None of the above-referenced Eriksson priority applications teaches or suggests the use of the PDGF-C growth factor domain in the absence of the N-terminal CUB domain, as required by the instant claims. Indeed, none of these priority applications teaches the approximate boundaries of the PDGF-C growth factor domain, nor otherwise suggests that PDGF-C contains an inhibitory N-terminal domain that, when cleaved by proteolytic processing, releases an activated form of PDGF-C corresponding to the polypeptide region as claimed.

Moreover, none of the above-referenced Eriksson priority applications teaches or suggests the use of a PDGF-C polypeptide for stimulating proliferation of connective tissue cells such as chondrocytes or osteoblasts, nor otherwise teaches or suggests the use of PDGF-C for promoting the growth of bone, ligament, or cartilage. In this respect, Applicants note that the Examiner relies on paragraph [0031] of Eriksson as stating that PDGF-C "has the ability to stimulate and/or enhance proliferation or differentiation and/or growth and/or motility of ... connective tissue cells." (Office Action at p. 5.) This disclosure, however, is not contained in any of the Eriksson priority applications filed prior to 12/7/98. (*See, e.g.*, provisional application nos. 60/102,461 [p. 5, 1st full para.]; 60/108,109 [p. 5, 2nd full para.]; and 60/110,749 [p. 5, 2nd full para.], where, in each case, Eriksson fails to disclose connective tissue cells as being among the cell types for PDGF-C-induced stimulation.)

For at least the reasons above, Eriksson does not anticipate the instant claims under 35 U.S.C. § 102(e). Withdrawal of the present rejection is therefore respectfully requested.

Rejections under 35 U.S.C. § 103(a)

Eriksson as evidenced by Camacho

Claim 7 stands rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Eriksson as evidenced by Camacho, as previously applied to claims 2-5, 8, 9, 11, 12, 22, 23, 25, and 26.

Applicants respectfully traverse this rejection insofar as it pertains to the present claims. Because independent claim 11 is patentable over Eriksson and Camacho for at least the reasons set forth above with regard to the rejection under § 102(e), claim 7, depending from claim 11, is also patentable over the cited references. Withdrawal of the rejection is therefore respectfully requested.

Eriksson, Camacho, and Bentz

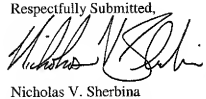
Claims 6 and 24 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Eriksson as evidenced by Camacho as previously applied to claims 2-5, 8, 9, 11, 12, 22, 23, 25, and 26, and further in view of EP 0512844 (Bentz *et al.*).

Applicants respectfully traverse this rejection insofar as it pertains to the present claims. As previously set forth, Eriksson's priority application nos. 60/102,461; 60/108,109; and 60/110,749 do not teach or suggest the use of the PDGF-C growth factor domain in the absence of the N-terminal CUB domain, as required by independent claim 11 and 22, nor do these priority applications teach or suggest the use of a PDGF-C polypeptide for stimulating proliferation of connective tissue cells such as chondrocytes or osteoblasts (claim 22), or for promoting the growth of bone, ligament, or cartilage (claim 11). Bentz *et al.* do not cure these deficiencies of Eriksson. Accordingly, claims 6 and 24, which depend directly from claims 11 and 22, are also patentable of the cited art. Withdrawal of the rejection is therefore respectfully requested.

CONCLUSION

On the basis of the above amendments and remarks, Applicants believe that each rejection has been addressed and overcome. Reconsideration of the application and its allowance are requested. If for any reason the Examiner feels that a telephone conference would expedite prosecution of the application, the Examiner is invited to telephone the undersigned at (206) 442-6752.

Respectfully Submitted,



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Enclosures:
Petition and Fee for Extension of Time

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